The Synthesis of Specifically and Selectively Deuteriated 4,4'-Bisalkoxyazoxybenzene Derivatives

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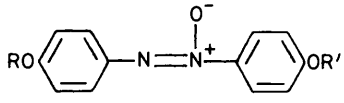
In connection with deuterium n.m.r. studies of molecular motion in liquid crystals we have developed a number of methods for the synthesis of selectively deuteriated 4,4'-bisalkoxyazoxybenzenes. This paper is concerned with (i) the labelling of specific methylene segments of the alkoxy-chains, (ii) the labelling of the aromatic nucleus, and (iii) the selective enrichment of the deuterium content of one alkoxy-chain relative to the other. Our studies of the n.m.r. spectra of these liquid crystals have shown that there is not (as has sometimes been supposed [1]) a monotonic decrease in C–D quadrupole splitting in passing from the oxygen to the CD_3 end of the alkoxy-chain. In [$^2H_6$]-PAA (*p*-azoxyanisole) we have also shown that the smaller splitting is associated with the CD_3O group nearest to the NO end of the azoxy-group. Whereas the photorearrangement of azoxy-compounds is normally regiospecific, the photorearrangement of PAA selectively deuteriated in one methoxy-group is unusual in that it leads to isotopically scrambled products.

Deuterium n.m.r. spectroscopy is being widely used [1] to characterise the long range orientational ordering of molecules in liquid crystals. The molecules of compounds (mesogens) which form thermotropic mesophases often consist of a rigid aromatic core to which one or more flexible alkyl or alkoxy-chains are attached. The 4,4'-bis(n-alkoxy)azoxybenzenes (1) are typical. At any point in the mesophase there is a preferred direction of orientation (the director) for these 'rod' shaped molecules and in an n.m.r. experiment the director will be aligned parallel to the direction of the applied magnetic field. If the molecules are perdeuteriated, each different C–D unit will contribute a resolved doublet to the deuterium n.m.r. spectrum. This doublet has its origin in the nuclear quadrupole–electric field gradient interaction and its magnitude is determined by the nuclear quadrupole coupling constant and the time-averaged angle between the C–D bond and the direction of the magnetic field. The latter depends upon both the internal conformational motion of the molecule and the reorientational motion of the conformers with respect to the director.[2] Provided the spectrum can be assigned, detailed information about these motions can be obtained. This requires the synthesis of specifically deuteriated mesogens. With few exceptions,[2] previous studies have been carried out on perdeuteriated materials. The need for specifically deuteriated mesogens has led us to develop appropriate synthetic methods. Such materials should also prove useful for ^{13}C n.m.r.[3] and Raman/i.r. spectroscopic [4] studies. This paper is concerned with the synthesis of specifically and selectively deuteriated azoxybenzenes (1) and, in particular, with three problems: (i) the labelling of specific methylene segments of the alkoxy-chains R and R'; (ii) the labelling of the aromatic nucleus; and (iii) selective enrichment of the deuterium content of one chain (R) relative to the other (R').



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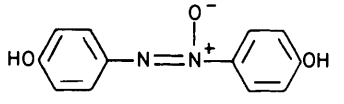

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(i) *The Labelling of Specific Methylene Segments of the Alkoxy-chains.*—Chain-labelled alkoxyazoxybenzenes are normally prepared by alkylation of *p*-nitrophenol followed by reduction with sodium alkoxide–alcohol.[5,6] The problem with this route is exchange of alkoxy-chains in the reduction step between solvent and substrate.[6,7] Therefore, we have found it preferable to alkylate 4,4'-dihydroxyazoxybenzene (2) instead.[8] This is readily available from the reaction of *p*-quinone monoxime with tosyl chloride–pyridine.[9] This more direct route also has the advantage over the *p*-nitrophenol route that the labelled chain is carried through one fewer synthetic step. Preparation of required 1,1-dideuteriated alkyl halides presents no problem.[10] The corresponding carboxylic acid is reduced with lithium aluminium deuteride and the resultant [1,1-$^2H_2$]alcohol treated with hydrobromic acid. The route to 2,2-dideuteriated alkyl halides is also well established.[10] It involves synthesis of the α,α-dideuteriated carboxylic acid (4) *via* the trideuteriated malonic acid (3), reduction with lithium aluminium hydride and treatment with hydrobromic acid. 3,3-Dideuteriated alkyl halides were prepared by a modification of these two routes in which a 1,1-dideuteriated alkyl halide was condensed with diethyl malonate to give the ester (5) which was hydrolysed, decarboxylated, reduced with lithium aluminium hydride and converted into the bromide in the usual manner. Specific deuteriation of the chain beyond this point presents a more interesting problem. One solution, employed by Djerassi,[10] is to extend the method employed for 3,3-dideuteriated systems. The normal preparative routes to 1,1- and 2,2-dideuteriated alkyl halides are used and then the functionally substituted end of the chain is extended in two carbon units by a series of malonic ester condensations. This, however, involves a large number of synthetic steps, a low overall yield, and in the present case (where *ca.* 200 mg quantities of the pure final products were required for the n.m.r. studies) it would have involved impractically large amounts of deuteriated starting materials. Another possible solution, employed with some success for the labelling of lyotropic liquid crystals, is the pairwise deuteriation of segments by catalytic reduction of a suitable acetylenic precursor with deuterium gas.[11] The problems which we have found with this method are two-fold. Firstly, not all of the desired acetylenic precursors are equally easy to prepare and, more seriously, there is competition between the desired specific catalytic acetylene reduction and

$RCD(CO_2D)_2$ (3)

RCD_2CO_2H (4)

$RCD_2CH(CO_2Et)_2$ (5)

$HO_2C(CH_2)_nCO_2Me$ (6)

RCD_2CD_2R (7)

$RCD_2(CH_2)_nCO_2Me$ (8)

$MeO_2C(CH_2)_{2n}CO_2Me$ (9)

$CD_3(CH_2)_nCO_2Me$ (10)

$CH_2{=}CH(CH_2)_{n-2}CO_2Me$ (11)

non-specific catalyst-mediated deuterium–CH_2 exchange with the rest of the alkyl chain. This leads to products which are not ' cleanly ' labelled and, particularly in cases where n.m.r. signals overlap, this can lead to results which are not wholly unambiguous. The best solution to the problem which we have found is to prepare the specifically deuteriated chains by a mixed Kolbé reaction.[12,13] Electrolysis of a mixture of the salt of an α-deuteriated acid (4) (R = D or alkyl) and the salt of the half-ester (6) ($n \geqslant 2$) gives a mixture consisting mainly of the three products (7)—(9). Provided the half-ester is used in excess, the wastage of deuterium label by formation of the hydrocarbon (7) is minimised. The mixture of products is normally easy to separate. The only problems which we have found are with olefinic by-products and here the chromatographic separation is only really difficult when making terminally deuteriated chains.[14] In this case the product (10) and the olefinic by-product (11) have similar chromatographic properties. Care must be taken, however, not to allow small amounts of this olefinic material to carry through to the final liquid crystal product since separation at that stage is almost impossible. In other cases no difficulties were experienced in removing the olefinic by-products, presumably because their chain-lengths are considerably shorter than that of the desired ester. The n.m.r. results of our studies on chain deuteriated bis(heptyloxy)-[2a] and bis(octyloxy)-[2b] azoxybenzene and some of those for octylcyanobiphenyl [2c] have already been published in preliminary form. Typical results are shown in Figure 1. Although the general trend is as expected with the ' most ordered ' CD_2 next to the aromatic nucleus giving the largest splitting and the ' least ordered ', terminal CD_3 the smallest splitting the trend is not, as has often been assumed, monotonic.[1] In particular there is an unexpected increase in splitting in passing from methylene-3 to methylene-4.

(ii) *Specific Deuteriation of the Aromatic Nucleus.*—Preparations of nuclear deuteriated 4,4′-bis(n-alkoxy)azoxybenzenes have normally been based on a synthesis of the corresponding ring-deuteriated 4-alkoxynitrobenzene followed by reduction.[8,15] Since we have found that direct alkylation of 4,4′-azoxyphenol (2) is also a convenient route to 4,4′-bis-(n-alkoxy)azoxybenzenes it seemed reasonable to suppose that a synthesis of ring-deuteriated 4,4′-azoxyphenol (2) would provide a convenient route to these compounds labelled with deuterium in the aromatic nucleus. However,

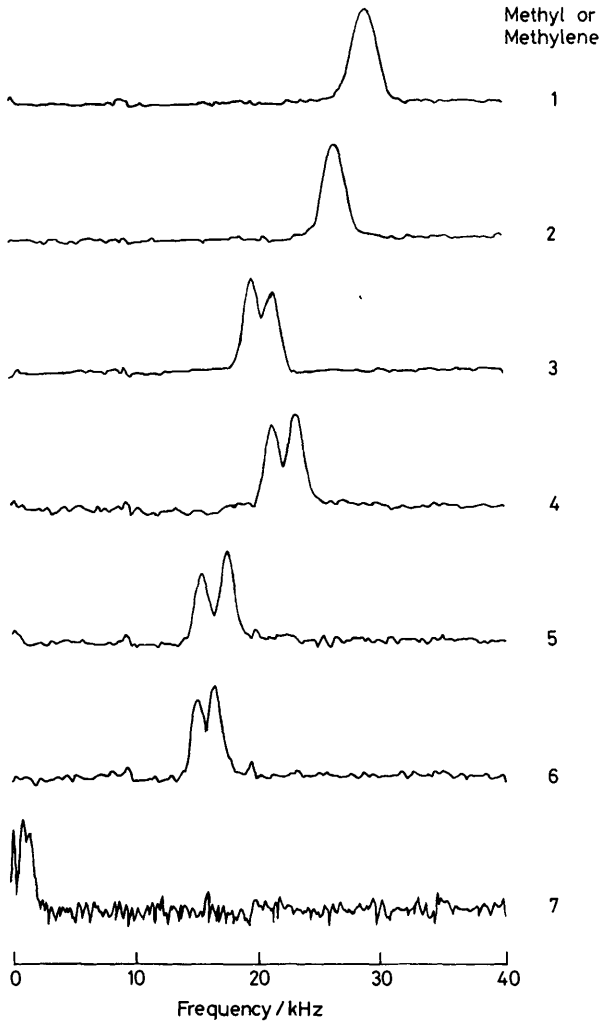
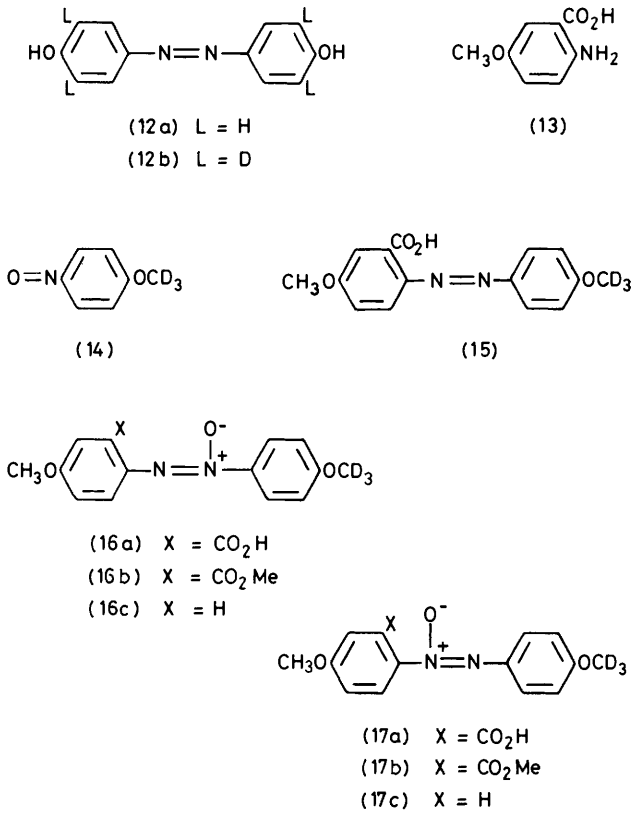


Figure 1. The deuterium n.m.r. spectra of each isomer of 4,4′-bis([$^2H_2$ or $^2H_3$]heptyloxy)azoxybenzene in the nematic phase at 382 K. Each spectrum is symmetric about zero frequency and only the high-field half of each doublet (or pair of doublets) is shown. (The numbering system used here is that conventionally used by organic chemists and used throughout this paper. In the literature of liquid crystals, however, numbering is frequently by ' segments ' starting from the aromatic nucleus. Under this system the oxygen is segment 1, methylene-1 is segment 2, *etc.*)

attempts to directly deuteriate the phenol (2) were unsuccessful, conditions which lead to deuterium incorporation also leading to extensive decomposition. Similar attempts to prepare the compounds starting from [2,4,6-$^2H_3$]phenol [16] were also unsuccessful. Nitrosation of phenol is known to have an exceptional high primary isotope effect [17] and this seems to slow quinone monoxime formation sufficiently to allow other reactions to compete. The best route which we have found is to use *p*-azophenol (12a). This can be easily prepared by fusing *p*-nitrophenol with potassium hydroxide [18] and cleanly converted into the tetradeuteriated compound (12b) by heating in a sealed tube with triethylamine–deuterium oxide. The 4,4′-dialkoxyazoxy-derivatives were then prepared by simple alkylation and oxidation.

(iii) *Selective Enrichment of the Deuterium Content of One Chain Relative to the Other.*—Some of the spectra in Figure 1 and the spectra for CD_3-labelled PAA (*p*-azoxyanisole)



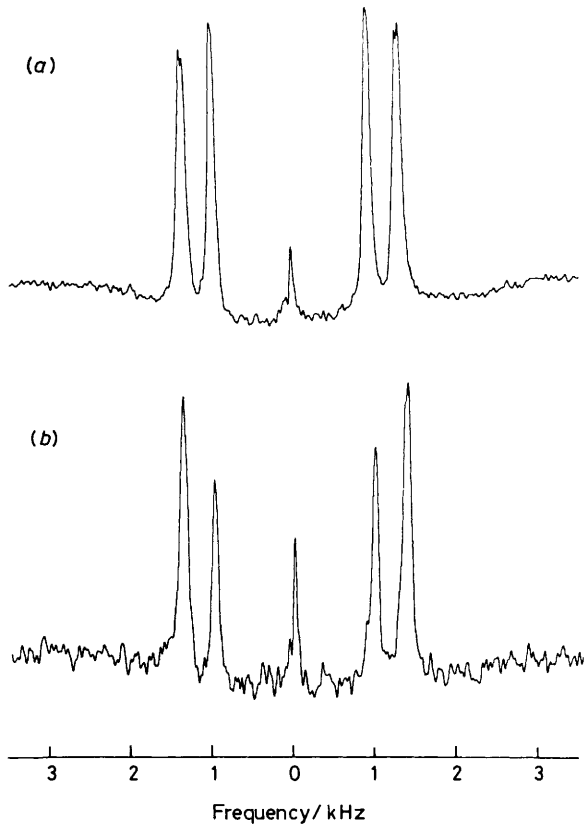


Figure 2. The proton decoupled deuterium n.m.r. spectra of (*a*) [$^2H_6$]-PAA and (*b*) a *ca.* 3 : 2 mixture of compounds (19c) and (20c). The compounds are in the nematic phase at 400 K. Spectra were obtained using the method of Emsley and Turner, *J. Chem. Soc., Faraday Trans. 2*, 1981, 1493

(Figure 2) show not one but two doublets. Clearly the alkyl chains at the ' N ' and ' NO ' ends of the molecule are inequivalent and to complete the assignment of the spectra (prior to modelling of the conformational behaviour) we needed to prepare compounds which are specifically or selectively deuteriated in one chain. So far this has only been completed for the PAA case. A number of methods exist for the synthesis of specific, unsymmetrical azoxybenzene derivatives [19,20] and our first synthesis was based on the method of Berwick and Rondeau.[20]

The acid-catalysed reaction between [$^2H_3$]methanol and quinone monoxime gave the deuteriated nitroso-compound (14) [21,22] in 24% yield. Condensation with the known amine (13) [23] gave the azo-compound (15) in low (7%) yield along with many other products. Berwick and Rondeau have shown that oxidation of this type of azo-compound, with a carboxylic acid residue in the *ortho*-position, results in a strong preference for oxygen introduction at the ' more remote ' nitrogen. Treatment of compound (15) with acetic acid–hydrogen peroxide gave a mixture of azoxy-compounds of which the major component is therefore assigned the structure (16a) and the minor component structure (17a). Decarboxylation by heating with copper in pyridine gave an 8 : 3 mixture of (16c) and (17c). The yield was low (24%) and although it could be increased by using longer reaction times this resulted in increasing interconversion of the two products. The mass spectrum showed the expected peak at *m/e* 124 (84%, $CD_3OC_6H_4N)^+$ for the major component (16c) and *m/e* 121 (32%, $CH_3OC_6H_4N)^+$ for the minor component (17c).[24] The effect of shift reagent on the ^1H n.m.r. spectrum of the products was at first surprising. Treatment of a CCl_4 solution with Eu(fod)$_3$ reagent splits the CH_3O signal. The CH_3O signal of the major component appears *downfield* to that of the minor component (Figure 3a). Since the shift reagent is thought to complex to the oxygen of the azoxy-group in these compounds and since the major component has its CH_3O group further from the azoxy-oxygen than the minor compound, this is, at first sight, the reverse of what would be expected. However, the direction of the contact shift produced by lanthanide reagents is not only a function of distance but also of angle to the metal–substrate bond. Whereas the aromatic ring protons are clearly in the deshielding zone and show the expected downfield shift, models show that the methoxy-groups will be close to the shielding–deshielding changeover point.[25] Figure 3 confirms this point, the shift reagent producing an upfield shift for one methoxy-group and a downfield shift for the other. Hence shift reagents are useful in these compounds as a method for analysing the composition of mixtures but must be used with caution for structural assignments. As expected the reverse effect is obtained with the Pr(fod)$_3$ reagent (major component CH_3O signal *upfield* to that of the minor component). Whereas this ' carboxylic acid ' route undoubtedly produced selectively deuteriated PAA the yields were very low and so a simpler method was developed which produced a lower selectivity but which was much more suitable for the production of large quantities of [$^2H_3$]-PAA, also having the advantages of being shorter and of carrying the deuterium label through fewer steps.

p-Anisidine was converted into its diazonium salt and coupled to the sodium salt of phenol to give the phenol (18a) which was converted into its acetate (18b). Oxidation of unsymmetrical *p*-substituted azo-compounds often gives a close to 1 : 1 mixture of products.[22] In this case, however, MeO and AcO are sufficiently different in their electronic effects that a

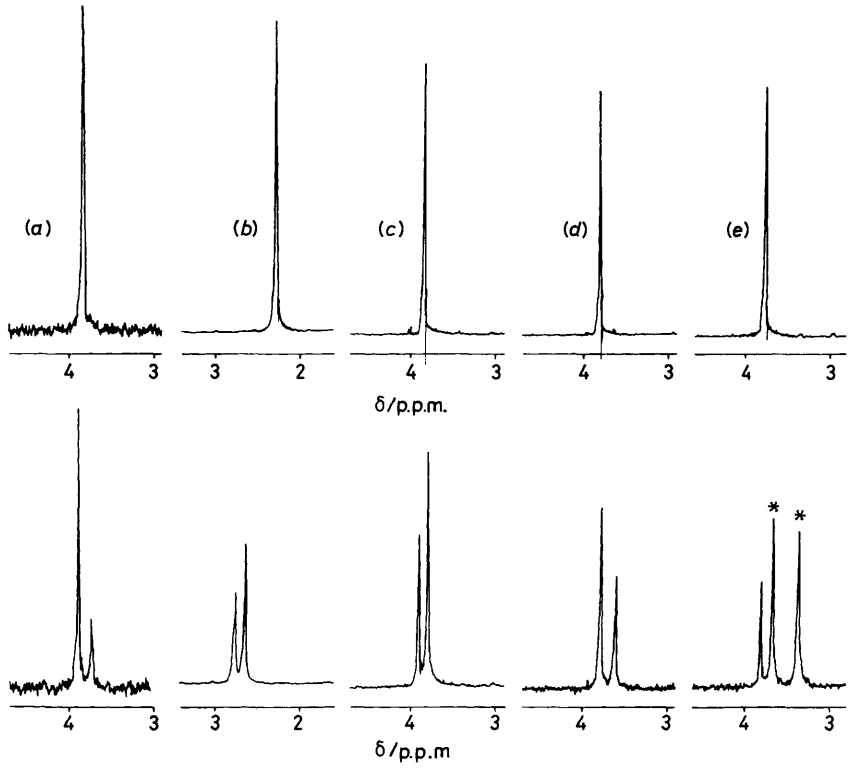


Figure 3. Effects of shift reagents on selected parts of the ^1H n.m.r. spectra of mixtures of azoxy-compounds (in carbon tetrachloride). In each case the upper trace shows the spectrum before adding the shift reagent and the lower trace the spectrum after: (*a*) *ca.* 8 : 3 mixture of (16c) and (17c) produced *via* the first synthetic route + $Eu(fod)_3$; (*b*) *ca.* 3 : 2 mixture of (19b) and (20b) produced *via* the second synthetic route + $Eu(fod)_3$; (*c*) *ca.* 3 : 2 mixture of (19c) and (20c) produced *via* the second synthetic route + $Eu(fod)_3$; (*d*) as in (*c*) + $Pr(fod)_3$; and (*e*) *ca.* 1 : 1 mixture of (21a) and (21b) produced by the photolysis of a *ca.* 3 : 2 mixture of (19c) + (20c), + $Pr(fod)_3$. The methoxy-resonances are identified with an asterisk

ca. 3 : 2 mixture of (19a)–(20a) results. The acetate can be removed under mild conditions (dilute NaOH in MeOH at room temperature) and CD_3 introduced by reaction of the phenol with base and [$^2H_3$]methyl iodide. The result is a *ca.* 3 : 2 mixture of azoxy-compounds (19c)–(20c). The mass spectrum confirms that (19c) is the predominant isomer (*i.e.* the reverse of the enrichment produced by the first route) and, as expected, the $Eu(fod)_3$-shifted n.m.r. spectrum shows the resonance for the MeO of the major component upfield to that of the minor component [also the reverse of the pattern for the mixture of azoxy-compounds produced by the first route (Figure 3c)]. A comparison of the proton decoupled deuterium n.m.r. spectrum of the neat nematic phase of this mixture with that of [$^2H_6$]-PAA is shown in Figure 2. From this it is clear that the smaller splitting is associated with the CD_3O group nearest to the NO of the azoxy-group.

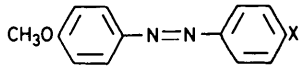
Although it is clear that the first synthetic route produced a mixture in which (16c) is the dominant isomer (based on the CO_2H directive effect and the mass spectroscopic evidence) and the second route one in which (19c) is the dominant isomer (based mainly on the mass spectral evidence), at an early stage of this work an attempt was made to confirm this by chemical degradation. Whilst this failed the result is of some interest. Whereas it is known that, for the acid-catalysed Wallich rearrangement, N–N oxygen scrambling is faster than N–C oxygen transfer,[26] some evidence in the literature suggested that the reverse was true for the photochemical equivalent of the Wallich rearrangement [27] and this was used as the basis for the attempted degradation. A *ca.* 3 : 2 mixture of compounds (19c)–(20c) was photolysed to give a mixture of (21a) and (22a).[28] The free OH was methylated (diazomethane) the central N–N bond cleaved reductively (Raney nickel–hydrogen) and the resultant amines acetylated and purified. Since the rearrangement involves oxygen transfer from nitrogen to the more remote aromatic ring [*i.e.* (19c) ⟶ (21a) and (20c) ⟶ (22a)] it was anticipated that the dimethoxylated acetanilide (23) would contain more [$^2H_3$]material than the monomethoxylated acetanilide (24). In the event almost equal mixtures of (23a) and (23b) and of (24a) and (24b) were obtained showing that, in this photochemical rearrangement, N–N oxygen transfer must be faster than N–C oxygen transfer or that oxygen transfer is also occurring to the adjacent aromatic ring. Whilst this scrambling is unusual for a photochemical rearrangement of an aromatic azoxy-compound it is not entirely without precedent.[27b]

Experimental

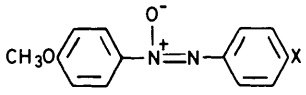
Unless otherwise stated all n.m.r. spectra refer to $CDCl_3$ solutions.

Details of the n.m.r. experiments on neat liquid crystalline samples have been given elsewhere.[2] The spectra shown in Figure 2 were recorded on a CXP-200 spectrometer (Southampton University). Ether refers to diethyl ether.

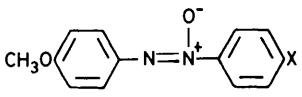
4,4′-*Bis*([1,1-$^2H_2$]*octyloxy*)*azoxybenzene*.[10]—Tetrahydrofuran (THF) (*ca.* 50 ml) was dried with lithium aluminium hydride (LAH) and distilled into a flask containing lithium aluminium deuteride (LAD) (0.8 g, 0.02 mol). Octanoic acid (2.88 g, 0.02 mol) was added slowly and the resulting mixture stirred and refluxed for 2 h. Water (*ca.* 50 ml) was added to



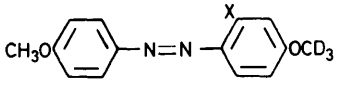
(18a) X = OH
(18b) X = $OCOCH_3$



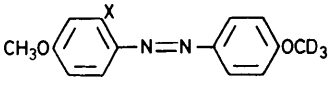
(19a) X = $OCOCH_3$
(19b) X = OH
(19c) X = OCD_3



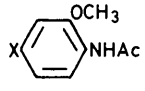
(20a) X = $OCOCH_3$
(20b) X = OH
(20c) X = OCD_3



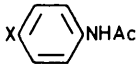
(21a) X = OH
(21b) X = OMe



(22a) X = OH
(22b) X = OMe

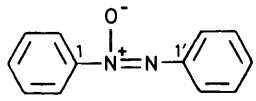


(23a) X = OCH_3
(23b) X = OCD_3



(24a) X = OCH_3
(24b) X = OCD_3

remove the excess of LAD and dilute sulphuric acid to decompose the resulting precipitate. The mixture was extracted with ether, the extract washed with sodium hydrogen carbonate and dried ($MgSO_4$). Removal of the solvents by rotary evaporation and suction on an oil pump left [1,1-$^2H_2$]octanol (2.63 g, 0.0196 mol), which was added to a stirred mixture of hydrobromic acid (13.3 g, equivalent to 0.078 mol hydrogen bromide) and concentrated sulphuric acid (1.93 g, 0.0196 mol). After refluxing for 6 h, water was added and the mixture extracted with ether. The extract was washed with sodium hydrogen carbonate, water, and then sodium hydrogen carbonate, dried ($MgSO_4$) and the solvent removed by rotary evaporation to give [1,1-$^2H_2$]octyl bromide (3.43 g, 87% yield) as a deep brown liquid; the g.l.c. retention time was the same as the undeuteriated compound. The absence of a triplet centred at δ 3.45 in the n.m.r. spectrum showed that the α-methylene was deuteriated. [1,1-$^2H_2$]Octyl bromide (3.43 g, 0.017 mol), 4,4′-dihydroxyazoxybenzene (2) [9] (1.3 g, 0.0057 mol), and potassium carbonate (3.13 g, 0.023 mol) in cyclohexanone (50 ml) were stirred and heated under reflux for 3 h.[6,7] The reaction mixture was allowed to cool and the cyclohexanone was decanted off the potassium carbonate, which was then washed with ether. The combined solutions were washed with dilute hydrochloric acid, sodium hydroxide and water, dried



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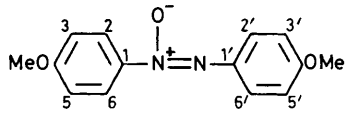

(26)

($MgSO_4$) and the solvents removed on a rotary evaporator. Column chromatography on a silica-gel column, with chloroform–light petroleum (b.p. 30—40 °C) as eluant, followed by recrystallization from absolute ethanol yielded 4,4′-bis-([1,1-$^2H_2$]octyloxy)azoxybenzene (0.985 g, 26%) as yellow plate-like crystals. It was shown to be homogeneous by t.l.c. and its R_F was identical with that of the undeuteriated material. Transition temperatures, 77.9 (C–S), 104.6 (S–N), 124.5—125 °C (N–I) [lit.(undeuteriated material) [29] 79.5, 107.5, 126.1 °C]. Essentially the same methods were used to prepare 4,4′-bis([1,1-$^2H_2$]heptyloxy)azoxybenzene, [1,1-$^2H_2$]pentyl bromide, and [1,1-$^2H_2$]hexyl bromide.

4,4′-*Bis*([2,2-$^2H_2$]*octyloxy*)*azoxybenzene*.[10]—Following the procedure of Katoh *et al.*, sodium (1.66 g, 0.072 mol) was added to a solution of diethyl n-hexylmalonate (7.32 g, 0.03 mol) in LAH-dried ether (100 ml). After stirring and refluxing the mixture for 1 h, absolute ethanol (0.55 g, 0.012 mol) was added. The reflux was continued for *ca.* 80 h, then the reaction mixture was cooled in ice, and deuterium oxide (30 ml) was added. The solvent was removed on a rotary evaporator and the residue dried *in vacuo*, leaving a yellow solid. A second portion of deuterium oxide (30 ml) was added, the mixture cooled in ice, and phosphorus trichloride (11.5 g, 0.084 mol) added slowly, dropwise. Following an overnight reflux, the product (4.58 g) was isolated by ether extraction, as an orange liquid. Its n.m.r. spectrum did not have a peak at δ 2.3 indicating that the α-methylene had been deuteriated. It was used without further purification in the next step. In a similar manner to the previous preparation [2,2-$^2H_2$]octanoic acid (4.58 g, 0.031 mol) was reduced with LAH (1.2 g, 0.03 mol) in ether (50 ml) to [2,2-$^2H_2$]octanol (3.15 g, 80%). Bromination of this with hydrobromic acid (9.4 g, 0.096 mol HBr) and concentrated sulphuric acid (2.35 g, 0.024 mol) yielded [2,2-$^2H_2$]octyl bromide (4.0 g, 86%) which was used to alkylate *p*-azoxyphenol (1.56 g, 0.0068 mol). The crude product was purified by column chromatography on silica gel with 50% chloroform–light petroleum (b.p. 30—40 °C) as eluant, and recrystallization from absolute ethanol to give 4,4′-bis([2,2-$^2H_2$]octyloxy)azoxybenzene (1.68 g, 36%) as yellow crystals. The R_F was identical with the undeuteriated material. Transition temperatures 77.8, 106.5—107.5, and 125.5—126 °C, δ_H 3.35 (4 H, s, CD_2CH_2O). Essentially the same method was used for the preparation of 4,4′-bis([2,2-$^2H_2$]heptyloxy)azoxybenzene.

4,4′-*Bis*([3,3-$^2H_2$]*octyloxy*)*azoxybenzene*.[10]—[1,1-$^2H_2$]-Hexyl bromide (11.68 g) was treated with the sodium salt of diethyl malonate [from diethyl malonate (11.54 g, 0.072 mol) and sodium (1.61 g, 0.07 mol)] in ethanol (35 ml) to give diethyl [1,1-$^2H_2$]hexylmalonate (8.36 g, 49%), b.p. 120—130 °C/1 mmHg. The ^1H n.m.r. spectrum of diethyl [1,1-$^2H_2$]-n-hexylmalonate had no signal at δ 1.6—2.1 and a singlet at δ 3.3 [$CD_2CH(CO_2Et)_2$]. In a similar way to the preparation of [2,2-$^2H_2$]octanoic acid the malonate ester was transformed

into its sodium salt, by reaction with sodium (1.88 g, 0.08 mol in 150 ml ether) and ethanol (0.63 g, 0.014 mol). The sodium salt was hydrolysed (35 ml water) and decarboxylated (35 ml water and 13 g, 0.095 mol phosphorus trichloride) yielding [3,3-$^2H_2$]octanoic acid (5.16 g, 97% without purification). This was reduced with LAH (1.25 g, 0.033 mol in 100 ml ether) to [3,3-$^2H_2$]octanol which was brominated (22.95 g hydrobromic acid and 3.33 g conc. sulphuric acid) to [3,3-$^2H_2$]octyl bromide (4.137 g, 62.5%). Alkylation of 4,4'-dihydroxyazoxybenzene (1.5 g, 6 mmol) in cyclohexanone (100 ml) catalysed by potassium carbonate (3.86 g, 0.028 mol) yielded 4,4'-bis([3,3-$^2H_2$]n-octyloxy)azoxybenzene (0.455 g, 10%) after purification by column chromatography and two recrystallizations from absolute ethanol. Transition temperatures 79.7, 108.2—108.7, and 126.8—127 °C. 4,4'-Bis([3,3-$^2H_2$]heptyloxy)azoxybenzene was prepared by essentially the same method.

4,4'-Bis([4,4-$^2H_2$]octyloxy)azoxybenzene.—[2,2-$^2H_2$]Hexanoic acid was prepared as described above and distilled. It was found that distillation of the α-deuteriated acid was essential to free it from phosphorus impurities which otherwise greatly reduced the yield in the electrochemical step. It was also important to distil under reduced pressure and at a fairly low temperature. Distillation of [2,2-$^2H_2$]hexanoic acid at atmospheric pressure and 200—210 °C, for example, resulted in exchange and in significant loss of deuterium from the α-position. Sodium (0.061 g, 2.6 mmol) was added to methanol (40 ml) in a jacketed, water-cooled electrolysis cell with horizontally mounted platinum electrodes and stirred by a magnetic stirrer. After it had dissolved, methyl hydrogen succinate (14.52 g, 0.110 mol) and [2,2-$^2H_2$]hexanoic acid (2.62 g, 0.022 mol) were added and the resulting solution electrolysed at a current of 0.65 A and 30 V. The potential of the (top) working electrode relative to a standard calomel electrode was monitored by use of a KCl–gelatin bridge, one end of which was close to the working electrode surface. It was maintained at $> +2$ V throughout the electrolysis. Since it is known that the Kolbé electrolysis is remarkably insensitive to anode potential (provided this is $\geq +2$ V) no attempt was made to work under potentiostatic conditions. After 15 h, the reaction mixture was neutral to litmus. The neutral product (9.2 g) was isolated and fractionally distilled to remove the main by-products which were expected to be methyl propionate, methyl propenoate, and dimethyl adipate. Purification was completed by column chromatography on kieselgel eluting with 30% chloroform–light petroleum (b.p. 30—40 °C), yielding methyl [4,4-$^2H_2$]octanoate (1.02 g, 29%) with the same t.l.c., R_F and g.l.c. retention time as the unlabelled analogue. Methyl [4,4-$^2H_2$]octanoate (1.02 g, 6.4 mmol) was reduced with LAH (0.241 g, 6.4 mmol), in a similar way to the reduction of octanoic acid, to give [4,4-$^2H_2$]octanol (0.585 g, 69%) which was then converted into [4,4-$^2H_2$]octyl bromide (0.793 g, 92%) in the usual manner. The bromide was used to alkylate 4,4'-dihydroxyazoxybenzene (0.312 g, 1.36 mmol) in the presence of potassium carbonate (0.748 g, 5.4 mmol) in cyclohexanone (50 ml). After purification of the crude yield by column chromatography on kieselgel, and two recrystallizations from absolute ethanol, 4,4'-bis([4,4-$^2H_2$]octyloxy)-azoxybenzene (0.17 g, 18%) was obtained as yellow crystals. Transition temperatures 75.5, 105.5—106.5, and 123—124 °C. Essentially the same method was used to prepare 4,4-bis([5,5-$^2H_2$]octyloxy)azoxybenzene, 4,4'-bis([6,6-$^2H_2$]-octyloxy)azoxybenzene, 4,4'-bis([7,7-$^2H_2$]octyloxy)azoxybenzene, 4,4'-bis([8,8,8-$^2H_3$]octyloxy)azoxybenzene, 4,4'-bis-([4,4-$^2H_2$]heptyloxy)azoxybenzene, 4,4'-bis([5,5-$^2H_2$]heptyloxy)azoxybenzene, 4,4'-bis([6,6-$^2H_2$]heptyloxy)azoxybenzene, and 4,4'-bis([7,7,7-$^2H_3$]heptyloxy)azoxybenzene.

[3,3',5,5'-$^2H_4$]-4,4'-Bis(heptyloxy)azoxybenzene.—4,4'-Dihydroxyazobenzene (12a) [18] (2 × 500 mg) [δ_H (acetone) 7.84 (4 H, d, *J* 9 Hz, 2-, 2'-, 6-, 6'-H) and 7.01 (4 H, d, *J* 9 Hz, 3-, 3'-, 5-, 5'-H)] was sealed in two Carius tubes each containing deuterium oxide (5 ml) and triethylamine (5 ml). These were heated at 160 °C for 2 days, cooled, opened, and the contents acidified and extracted with ether (2 × 150 ml). The ether extracts were dried and evaporated to give the crude [3,3',5,5'-$^2H_4$]-4,4'-dihydroxyazobenzene (12b) (900 mg, 90%); δ_H (acetone) 7.84 (4 H, s, 2-, 2'-, 6-, 6'-H); *m/e* 218 (M^+, 88%) 123 ($HOC_6H_2D_2N_2^+$, 39), and 95 ($HOC_6H_2D_2^+$, 100). This was used without further purification. The phenol (900 mg), heptyl bromide (3 g), cyclohexanone (30 ml), and potassium carbonate (1 g) were refluxed together for 18 h. The reaction mixture was acidified and partitioned between water and ether. The ether solution was dried ($MgSO_4$), silica added and the solvent removed on a rotary evaporator. The product thus absorbed on silica was transferred to a silica chromatography column which was eluted with 3% methanol–chloroform. The 4,4'-bis(heptyloxy)azobenzene thus obtained was refluxed with peracetic acid (2 ml) in methylene dichloride (100 ml) for 6 h. The methylene dichloride solution was washed with dilute aqueous sodium hydroxide and water, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed on silica eluting first with 1 : 1 chloroform–light petroleum (b.p. 30—40 °C) and then with chloroform to yield [3,3',5,5'-$^2H_4$]-4,4'-bis(heptyloxy)azoxybenzene (750 mg, 42% based on azophenol) which was recrystallised three times from ethanol, transition temperatures 74—75 (C–S), 93—94 (S–N), and 123—124 °C (N–I) [lit., (undeuteriated material) [29] 75, 95, and 124 °C); δ_H 7.89 (4 H, s, 2-, 2'-, 6-, 6'-H), 4.04 (4 H, t, *J* 7 Hz, CH_2O), and 2.6—0.7 (26 H, m, remaining CH_2 and CH_3), *m/e* 430 (M^+). [3,3',5,5'-$^2H_4$]-4,4'-Bis(octyloxy)azoxybenzene was prepared by essentially the same method.

Selectively Deuteriated 4-Methoxy-4'-[$^2H_3$]methoxyazoxybenzene [Mixture of (16c) and (17c)]. Route A.—Concentrated sulphuric acid (0.2 ml) was added dropwise to a stirred mixture of dry quinone monoxime [9] (6.5 g), toluene (7.25 ml), and [$^2H_3$]methanol (5 ml) under nitrogen and surrounded by a water bath at 50 °C. There was an initial exothermic reaction. After 1 h at 50 °C, 2M-sodium hydroxide (3 ml) and toluene (10 ml) were added and the solvent removed using a rotary evaporator. The residue was extracted several times with boiling pentane (until the extracts were no longer green). The pentane was removed by gentle warming in a stream of nitrogen to yield 1-[$^2H_3$]methoxy-4-nitrosobenzene (14) (1.74 g, 24%) as bright green needles which melted just above room temperature (lit.,[22] m.p. 23 °C); δ_H 7.02, 7.92 (each 2 H, doublets, *J* 9 Hz, ArH). Undeuteriated samples also showed a 3 H singlet at δ 3.95. 2-Amino-5-methoxybenzoic acid (13) (2.32 g) [23] was then dissolved in glacial acetic acid (15 ml) with gentle warming. This solution was added to 1-[$^2H_3$]methoxy-4-nitrosobenzene (1.74 g) and the mixture, under nitrogen, was heated on a steam bath for 45 min and then allowed to stand at room temperature for 18 h by which time t.l.c. examination showed no remaining amine. The solvent was removed under reduced pressure and the residue chromatographed on kieselgel to yield many coloured products including 4,4'-bis-([$^2H_3$]methoxy)azoxybenzene (180 mg, 6%) and 4-methoxy-4'-[$^2H_3$]methoxyazobenzene-2-carboxylic acid (15) as a pale yellow solid (250 mg, 7%), m.p. 167—169 °C. A similar preparation using undeuteriated 1-methoxy-4-nitrosobenzene gave the *undeuteriated acid* which was recrystallised from ethanol, m.p. 168—169 °C (Found: C, 63.0; H, 4.8; N, 9.7%; M^+, 286.0949. $C_{15}H_{14}N_2O_4$ requires C, 62.9; H, 4.9; N, 9.8%; M^+, 286.0953); δ_H 3.92, 3.96 (each 3 H, s, OMe), 7.03, 7.91 (each 2 H, d, 2'-, 3'-, 5', 6'-ArH), 7.1—7.3 (1 H, m, 5-ArH),

7.7—8.1 (2 H, m, 3-, 6-ArH), and 13.8 (1 H exchanged with D_2O, s, CO_2H); *m/e* 286 (M^+, 38%) and 107 ($MeOC_6H_4^+$, 100). 4-Methoxy-4′-[$^2H_3$]methoxyazobenzene-2-carboxylic acid (15) (250 mg) was treated with peracetic acid (40% w/v, 15 ml) and 5 drops of concentrated sulphuric acid. Chloroform (*ca.* 5 ml) was added to give a homogeneous solution. After 18 h, t.l.c. showed that most of the starting material had been consumed. The mixture was poured into ice and extracted with ether (250 ml). The ether extracts were washed with water (4 × 250 ml), dried ($MgSO_4$), filtered, evaporated under reduced pressure and chromatographed on kieselgel eluting with chloroform to give recovered starting material (16 mg) and a mixture of the α- and β-oxides of 4-methoxy-4′-[$^2H_3$]-methoxyazobenzene [(16a) and (17a)] as a yellow powder (145 mg, 55%), m.p. 137—146 °C.

A small sample of this mixture of acids was methylated with diazomethane and the resultant mixture of α- and β-oxides of 2-methoxycarbonyl-4-methoxy-4′-[$^2H_3$]methoxyazobenzene [(16b) and (17b)] was purified by chromatography on kieselgel eluting with chloroform; δ_H 3.86, 3.90 (each 3 H, s, OMe) and 6.9—8.4 (7 H, m, ArH). Addition of Eu(fod)$_3$ reagent failed to split the MeO resonances and so gave no information on the proportion of α- and β-isomers. As expected [24] the mass spectrum was dominated by CO_2Me-based fragmentations, but the relative abundances of the *m/e* 110 and 165 peaks perhaps suggests a preponderance of isomer (16b) over (17b) [*m/e* 319 (M^+, 13%), 303 ($M^+ - O$, 5), 260 ($M^+ - CO_2Me$, 81), 179 ($C_9H_9NO_3^+$, 2), 165 ($C_9H_9O_3^+$, 19), 124 ($C_7H_4D_3NO^+$, 23), and 110 ($C_7H_4D_3O^+$, 100%)].

A portion of the mixed azoxycarboxylic acids (16a) and (17a) (50 mg), active copper (50 mg, freshly prepared by precipitation from copper sulphate with zinc dust), and a few crystals of copper(II) acetate in pyridine (2 ml) was refluxed for 2½ h. The solvent was removed under reduced pressure and the residue chromatographed on kieselgel eluting with chloroform to give recovered starting material (29 mg) and selectively deuteriated 4,4′-dimethoxyazoxybenzene (10 mg, 24%) which was recrystallised from ethanol to give yellow crystals (7 mg). Transition temperatures were identical with those quoted for the undeuteriated material. Both the mass spectrum and the Eu(fod)$_3$-shifted ^1H n.m.r. spectrum in CCl_4 (Figure 3a) suggested that this was a *ca.* 8 : 3 mixture of compounds (16a) and (17c). In the Eu(fod)$_3$-shifted spectrum the methyl resonance for the major component appeared downfield to that of the minor component. In the Pr(fod)$_3$-shifted spectrum it was upfield of that of the minor component; *m/e* 261 (M^+, 100%), 245 ($M^+ - 16$, 23), 124 ($C_7H_4D_3ON^+$, 83.6), and 121 ($C_7H_7ON^+$, 31.4). The mass spectrum of [$^2H_6$]-PAA under identical conditions showed no peak at *m/e* 121. A higher yield of [$^2H_3$]-PAA could be obtained by more prolonged heating but there was some evidence for loss of specificity in the labelling.

Selectively Deuteriated 4-*Methoxy*-4′-[$^2H_3$]*methoxyazoxybenzene* [*Mixture of* (19c) *and* (20c)]. *Route B.*—*p*-Methoxyaniline (6.1 g) in 2M-hydrochloric acid (100 cm^3) was cooled in ice–salt and sodium nitrite (4.7 g) was added in portions during 20 min, keeping the temperature of the solution between 0 and −5 °C. The solution was then mixed with an ice-cold solution of phenol (4.7 g) in 2M-sodium hydroxide (100 cm^3) and the mixture was acidified and filtered. The yellow-brown azo-compound thus obtained, in almost quantitative yield, was mainly the desired 4-hydroxy-4′-methoxyazobenzene (18a); δ_H (acetone) 7.84 (3 H, s, MeO), 6.8—8.0 (8 H, overlapping AB quartets, ArH), and 8.92 (1 H, s, OH). T.l.c. showed the presence of a less polar coloured impurity, probably the *ortho*-isomer, which was difficult to remove at this stage but which was readily removed after acetylation. Hence this phenolic product was used in its crude state. The phenol (18a) (1.0 g) in acetic anhydride (5 ml) with 1 drop of concentrated sulphuric acid was heated at 75 °C for 5 h. The mixture was partitioned between water and ether, the ether solution was washed with water and dilute sodium hydroxide, dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The residue was recrystallised from ethanol–water (1 : 1) to give 4-*acetoxy*-4′-*methoxyazobenzene* (18b) as orange-yellow needles (0.95 g, 80%), m.p. 119—122.5 °C (Found: C, 66.6; H, 5.3; N, 10.6. $C_{15}H_{14}N_2O_3$ requires C, 66.7; H, 5.2; N, 10.4%); δ_H 2.33 (3 H, s, CH_3CO_2), 3.90 (3 H, s, CH_3O), 7.07 and 7.30 (each 2 H, d, 3-, 5-, 3′-, 5′-ArH), and 8.02 (4 H, d, 2-, 6-, 2′-, 6′-ArH). A portion of the acetate (18b) (1 g) was treated with hydrogen peroxide–acetic acid (a 40 ml portion of a mixture of 100 ml of glacial acetic acid, 45 ml of 100 vol hydrogen peroxide and 1 ml of conc. sulphuric acid) and the mixture stirred for 16 h. The reaction mixture was poured into water (100 ml) and ether (100 ml). The orange ether layer was washed with water (5 × 100 ml), dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a *ca.* 3 : 2 mixture of the azoxy-compounds (19a) and (20a) (0.647 g, 61%), δ_H (CCl_4) 2.46 (3 H, s, $MeCO_2$), 3.83 (3 H, s, MeO), 6.8—7.5 (4 H, m, 3-, 3′-, 5-, 5′-ArH), and 8.2—8.6 (4 H, m, 2-, 2′-, 6-, 6′-ArH). Addition of Eu(fod)$_3$ splits the $MeCO_2$ resonance such that the signal for the minor component appears downfield of that of the major component (Figure 3b). This is consistent with the assignment (19a) > (20a) and although a similar attempt to assign the composition of a (19c)–(20c) mixture gave an anomalous result (see Discussion section) we believe this shift effect to be genuine since *both* resonances are shifted to low field. The mass spectrum tends to confirm the view that (19a) > (20a) but the spectrum is complicated by ester fragmentations and the ratio of the *m/e* 107 ($MeOC_6H_4^+$) and 135 ($AcOC_6H_4^+$) peaks is significantly higher than the product ratio suggested by the Eu(fod)$_3$ results for this mixture and subsequent transformation products. Also, only one of the nitrogen retaining fragments (*m/e* 121) is observed so the mass spectral evidence must be treated with some reservations; *m/e* 286 (M^+, 78%), 270 ($M^+ - O$, 42), 244 ($M^+ - CH_2CO$, 67), 228 ($M^+ - CH_2CO_2$, 40), 135 ($AcOC_6H_4^+$, 36), 121 ($MeOC_6H_4N^+$, 82), and 107 ($MeOC_6H_4^+$, 100); δ_C 21.07 (CH_3CO_2), 55.5, 55.6 (MeO), 113.7, 113.8, 121.7 (C-3, -3′), 124.0, 124.7, 126.8, 128.0 (C-2, -2′), 137.8, 141.6, 141.8, 145.6 (C-1, -1′), 150.6, 152.7, 160.6, 162.3 (C-4, -4′), and 168.8 and 169.0 (CH_3CO_2). A portion of the mixture of azoxy-compounds (19a) and (20a) (547 mg) was added to methanol (50 ml) and 2M-aqueous sodium hydroxide (35 ml) and the mixture was stirred for 2 h and then acidified and extracted with ether. The ether extracts were washed, dried, and evaporated to give a 3 : 2 mixture of the azoxy-compounds (19b) and (20b) (477 mg, 96%), δ_H 3.85 (3 H, s, MeO), 6.8—7.1 (5 H, m, 3-, 3′-, 5-, 5′-ArH and ArOH), 8.1—8.3 (4 H, m, 2-, 2′-, 6-, 6′-ArH); δ_C 54.5, 54.7 (MeO), 112.7, 114.4, 114.5 (C-3, -3′), 122.6, 122.8, 126.7, 127.1 (C-2, -2′), 135.9, 137.0, 139.4, 140.5 (C-1, -1′), 158.0, 159.0, 159.7, and 160.7 (C-4, -4′). A 3 : 2 mixture of the azoxy-compounds (19b) and (20b) (609 mg), [$^2H_3$]methyl iodide (0.4 ml), and potassium carbonate (1.38 g) in cyclohexanone (20 ml) was refluxed for 3 h. After the usual work-up the product was purified by chromatography on kieselgel eluting with 1 : 1 chloroform–light petroleum (b.p. 30—40 °C) and repeated crystallisation from ethanol. A *ca.* 3 : 2 mixture of the azoxy-compounds (19c) and (20c) was obtained (178 mg, 27%), transition temperatures 118—119 °C (C–N) and 135—136 °C (N–I) [lit., undeuteriated compound,[29] 118 and 136 °C]. The assignment of (19c) as the major isomer rests on the mass and ^1H n.m.r. spectra. In the Eu(fod)$_3$-shifted spectrum the methyl

resonance for the major component appeared upfield of that of the minor component (Figure 3c). A reverse effect was observed with $Pr(fod)_3$ (Figure 3d) (see Figure 3 and discussion in the main text), *m/e* 261 (M^+, 100%), 124 ($CD_3OC_6H_4N^+$, 42), and 121 ($CH_3OC_6H_4N^+$, 59).

We attempted to confirm our assignment of the major component of the mixture of azoxy-compounds (19a) and (20a) by ^{13}C n.m.r. spectroscopy. However, the assignment of the ^{13}C n.m.r. spectra of azoxy-compounds, in general, is poorly based. The only assignment which seems clear-cut is of the 1- and 1'-carbon atoms (δ 148.5 and 143.9, respectively) of compound (25) based on ^{15}N-^{13}C coupling constants.[30] Johnson and Jankowski [31] have also published a number of assignments including the following for azoxyanisole (26): δ_C 123.6 (C-2', -6'), 127.7 (C-2, -6), 160.1 (C-4), and 161.8 (C-4'). Since the basis of these assignments is not entirely clear we attempted to obtain confirmation. We studied the effect of $Eu(fod)_3$ on the ^{13}C n.m.r. spectrum of compound (26) in *ca.* 3 : 1 CCl_4–$CDCl_3$. Whereas this method may not be wholly reliable it suggests an assignment in agreement with that of Schotzer *et al.* for the 1,1' positions [30] but the reverse of that of Jacobs and Jankowski for positions 2, 4, 6, 2', 4', and 6'.[31] δ_C 54.8, 55.0 (MeO, downfield shift per mol of $Eu(fod)_3$ 0.8, 1.2 p.p.m.), 113.1 (C-3', 6.2), 13.3 (C-3, 6.7), 123.5 (C-2, 22.0), 127.5 (C-2', 16.0), 138.0 (C-1', 15.0), 141.7 (C-1, 26.0), 159.7 (C-4', 3.7), and 161.4 (C-4, 6.7). As a result it seems that only the assignment of the 1- and 1'-carbons is reliable. Using Schwotzer's assignment for the parent system and standard parameters for the effect of substituents [32] we predict the following pattern for a 3 : 2 mixture of (19a) and (20a): δ_C 138.0 (minor component), 138.4 (major component), 141.7 (major), and 142.4 (minor). The observed signal positions and intensities are 135.9 (minor), 136.9 (major), 139.4 (major), and 140.5 (minor). For a 3 : 2 mixture of (19c) and (20c) we predict δ_C 138.0 (minor), 141.7 (major), 143.5 (major), 147.1 (minor). We observed δ_C 137.9 (major), 141.4 (minor), 141.7 (major), and 145.5 (minor). These results can be seen as a weak confirmation of the assignments based on mass spectroscopy (and, of course, the synthetic route followed).

Attempted Chemical Degradation of Selectively Labelled 4-Methoxy-4'-[$^2H_3$]methoxyazoxybenzene.—A *ca.* 3 : 2 mixture of the deuteriated azoxy-compounds (19c) and (20c) (200 mg) in absolute ethanol (250 ml) was photolysed in a water-cooled silica reactor with a medium-pressure mercury lamp, under oxygen-free nitrogen, until no more starting material could be detected by t.l.c. (24 h). Silica was added to the solution and the solvent was removed on a rotary evaporator. The product, absorbed on silica, was transferred to the top of a silica chromatography column which was eluted with 20% chloroform–light petroleum (b.p. 30—40 °C). 2-Hydroxy-4(4')-methoxy-4'(4)-azobenzene was obtained [mixture of (21a) and (22a)] in quantitative yield (200 mg) and recrystallised from ethanol, m.p. 128—130 °C (lit.,[28] 133 °C); δ_H (CCl_4) 3.82 (3 H, s, MeO), 6.3—7.0 (4 H, m, 3-, 3'-, 5-, 5'-ArH), 7.5—7.9 (3 H, m, 6-, 6'-, 2'-ArH), and 13.20 (1 H, s, OH). Addition of $Pr(fod)_3$ reagent shifted the MeO resonances to higher field and they were split into two almost equal singlets (Figure 3d), suggesting that equilibration of the azoxy-compounds (19c) and (20c) successfully competed with the desired rearrangement, and this was confirmed by the subsequent degradation. Similarly the mass spectrum gave almost equal peaks at *m/e* 107 and 110; *m/e* 261 (M^+, 85%), 245 ($M^+ - 16$, 69), 154 ($CD_3C_6H_4N_2O_2^+$, 14), 151 ($CH_3C_6H_4N_2O_2^+$, 17), 138 ($CD_3C_6H_4N_2O^+$, 28), 135 ($CH_3C_6H_4N_2O^+$, 32), 126 ($CD_3C_6H_4O_2^+$, 23), 123 ($CH_3C_6H_4O_2^+$, 26), 110 ($CD_3C_6H_4O^+$, 100), and 107 ($CH_3C_6H_4O^+$, 99). The product from the photochemical reaction was dissolved in a little methanol and treated with an excess of ethereal diazomethane. After standing for 24 h at room temperature, the solvent was removed under reduced pressure and the residue chromatographed on silica eluting with 10% ether–light petroleum (b.p. 30—40 °C) to yield 2,4(4')-dimethoxy-4'(4)-[$^2H_3$]methoxyazobenzene [mixture of (21b) and (22b)] which was recrystallised twice from ethanol to give yellow needles (54 mg, 51%), m.p. 83—89 °C; δ_H 3.83 (3 H, s, 4,4'-MeO), 3.98 (3 H, s, 2-MeO), 6.4—7.0 (4 H, m, 3-, 3'-, 5-, 5'-ArH), and 7.6—7.9 (3 H, m, 2'-, 6-, 6'-ArH); *m/e* 275 (M^+, 51%), 245 ($M^+ - CH_2O$, 10), 168 ($CD_3C_7H_6N_2O_2^+$, 15), 165 ($CH_3{}^{-}{}_7H_6N_2O_2^+$, 17), 153 (15), 150 (22), 138 ($CD_3C_6H_4N_2O^+$, 15), 135 ($CH_3C_6H_4O^+$, 22), 125 (47), 122 (55), 110 ($CD_3C_6H_4O^+$, 75), and 107 ($CH_3C_6H_4O^+$, 100). A similar preparation from undeuteriated azoxyanisole gave *undeuteriated* 2,4,4'-*trimethoxyazobenzene*, m.p. 82—89 °C (Found: C, 66.4; H, 6.1; N, 10.0. $C_{15}H_{16}N_2O_3$ requires C, 66.2; H, 5.9; N, 10.3%). In the ^1H n.m.r. spectrum of the undeuteriated material the singlet at δ 3.83 integrates for a total of 6 H. The mixture of azo-compounds (21b) and (22b) (54 mg) in ethanol (5 ml) with a little freshly prepared Raney nickel was reduced with hydrogen at atmospheric pressure and room temperature.[33] After 2 days the mixture was filtered through Celite and the Celite washed through with ether. The combined filtrate and washings were extracted with 2M-hydrochloric acid (2 × 10 ml), the aqueous extracts were made basic with sodium hydroxide and re-extracted with ether. The ether extracts were dried and evaporated. The residue was heated on a steam bath with acetic anhydride (5 ml) for 30 min and poured into ice. The products were isolated by ether extraction and chromatographed on kieselgel (elution with ether) to give first 2,4-dimethoxyacetanilide (12 mg) which was recrystallised from aqueous ethanol, m.p. 113.5—114 °C (lit.,[34] m.p. 115—116 °C) and then 4-methoxyacetanilide (5 mg) which was also recrystallised from aqueous ethanol, m.p. 125—126 °C (lit.,[35] m.p. 130—132 °C). Both acetanilides proved to be almost 1 : 1 mixtures of the undeuteriated and the [$^2H_3$]-materials, showing in the first instance *m/e* 198 ($M^+ + {}^2H_3$, 46%) and 195 (M^+, 52) and in the second case *m/e* 168 ($M^+ + {}^2H_3$, 30%) and 165 (M^+, 28). The mass spectra of the undeuteriated acetanilides showed no significant $M \pm 3$ peak and so the intensities we obtained should directly reflect the ratio of $^2H_0$ and $^2H_3$ components.

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